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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/661,161	09/13/2000	Mary Chen	M-9181-2C US	2159

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	PAPER NUMBER
1651	5

DATE MAILED: 12/13/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/661,161	Chen et al.
Examiner	**Art Unit**
Vera Afremova	1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 30, 2001*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1 and 20-25* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1 and 20-25* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Claims 1 and 20-25 are pending and under examination. Claims 2-19 were canceled by applicants. [Preliminary amendment filed 9/13/2000, Paper No. 2].

Information Disclosure Statement

The information disclosure statement filed 9/13/2000 [Paper No. 3] has been considered and attached herein except for two references AR and AY for which no copies and/or no proper citations were provided. See 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37CFR 3.73(b).

1. Claims 1 and 20-25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2-16 and 23-26 of U.S. Patent No. 5,856,179 [IDS-AG]. Although the conflicting claims are not identical, they are not patentably distinct from

each other because they are directed to the similar methods of growing mammalian cells including CHO cells by maintaining glucose concentration between about 0.02 g/L and about 0.2 g/l and by using initial osmolarity of about 280-320 mOSm. The method of US '179 is broader because it encompasses the use of larger glucose concentration ranges and incorporation of additional steps in the method of growing/culturing animal cells. Thus, the methods as claimed are co-extensive.

2. Claims 1 and 20-25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of U.S. Patent No. 6,180,401 [A]. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are directed to similar method methods of growing mammalian cells including CHO cells by maintaining glucose concentration between about 0.02 g/L and about 0.2 g/l and by using initial osmolarity of about 280-320 mOSm. The method of US '401 [A] is broader because it encompasses the use of larger glucose concentration ranges and incorporation of additional nutrients such as glutamine in the method of growing/culturing animal cells. Thus, the methods as claimed are co-extensive.

Claim Rejections - 35 USC § 112

Claims 1 and 20-25 are rejected under 35 U.S.C. 112, *second paragraph*, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered indefinite by the phrase "inclusive" because the meaning of this limitation is unclear. Further, the claim 1 is rendered indefinite by the phrase "thereby controlling osmolarity" because it is uncertain if glucose is an osmolarity regulating agent. How is osmolarity controlled? To what level is osmolarity adjusted, when (if) controlled? Is an osmolarity during culturing step the same as a starting osmolarity of 280-330 mOsm?

Claim 1 and 21 are rendered indefinite by the phrases "about" because standard error for concentration range or cell density are uncertain and, thus, the low and upper amounts of the intended ranges can not be determined.

The claim 2 is rendered indefinite by the phrase "medium contains excess amino acids" because it is unclear in excess to what amount additional amino acids are required as claimed. The suitable medium as disclosed appears to be an animal culture medium known in the art (page 11, last par.).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 20-22, 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Glaken et al. [IDS-AT] or JP 1-101882 [IDS-AJ] in the light of Waymoth [IDS-BG].

The claims are directed to a method of growing animal cells in a fed batch system wherein the method comprises culturing the cells by controlling glucose concentration between about 0.02 -0.2 g/L during culturing. A starting osmolarity is 280-302 mOsm as intended. Some claims are further drawn to the use of initial cell density between about $3x10^5$ and $1.5x10^6$ cells/ml or to the use mammalian cells or to the use of animal cells comprising nucleic acid encoding polypeptide or the use of flow injection analysis for glucose control in the method of culturing animal cells.

Glaken et al. [IDS-AT] disclose a method of growing mammalian cells in a fed batch system (page 1388, col. 1, par. 2) wherein the method comprises culturing the cells in an animal culture medium by controlling glucose concentration of 0.1 mM or about 0.02 g/L during culturing (See culturing animal cells between 100 and 200 hours at Fig. 9). The cited reference clearly teaches an importance of lowering/adjusting glucose concentration until 0.1 mM during culturing period (page 1386, col. 1, par. 3) and the use of initial density or inoculum of mammalian cells of about $1.5x10^6$ cells/ml (page 1388, col.1, par. 1) which is between $3x10^5$ and $1.5x10^6$ cells/ml as presently claimed. The animal cells in the method of the cited reference comprise a nucleic acid encoding polypeptide such as DNA, for example. The cited reference teaches the use of on-line automated glucose control (fig. 2) as a glucose control by flow injection analysis of the claimed method (page 17, line 28).

JP 1-101882 [IDS-AJ] teaches a method of growing animal cells in a perfusion system wherein the method comprises culturing the cells by controlling glucose concentration above 0.01 mM but less than 3 mM (see translation page 3) which is between 0.02 -0.2 g/L as presently

claimed. And the cited reference teaches the use of initial cell density of $5x10^5$ cell/ml (translation page 7, par. 1) which is between $3x10^5$ and $1.5x10^6$ cells/ml as required for the claimed method. The perfusion system of the cited reference (translation page 4, par. 3) appears to be identical to the claimed fed-batch system in the light of substantially similar, if not identical, definitions which encompass supplying nutrients "continuously or in discrete increments" (current specification page 5, line 30). The animal cells of the cited reference are mammalian cells or mouse-human hybridoma which comprise nucleic acid encoding a polypeptide such as IgG1 (translation page 6, par. 2) as required for the cells of the claimed method.

Although the cited references do not exclusively disclose an initial osmolarity of about 280-302 mOsm for the culture media, they teach the use of regular animal media. And it is known that initial osmolarity of regular animal media or initial osmolarity of the majority of commercially available animal media is within the claimed range of 280-320 mOsm (see table 7 of the reference by Waymoth [IDS-BG]). Thus, the cited methods are reasonably expected to inherently comprise the use of identical initial osmolarity of the culture media as required for the presently claimed method.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glaken et al. [IDS-AT] or JP 1-101882 [IDS-AJ] in the light of Waymoth [IDS-BG] taken with Kurano et al. [IDS-BK] and Kurano et al. [IDS-BJ].

The claims 1, 20-22, 24 and 25 as explained above. The claim 23 is further dawn to the use of CHO cells in the claimed method of growing animal cells.

The reference Glaken et al. [IDS-AT] and JP 1-101882 [IDS-AJ] are relied upon as explained above for the disclosure of a method of culturing mammalian cells by maintaining glucose concentration between 0.02 -0.2 g/L in a fed batch system wherein the method encompasses the use of a regular animal culture medium with initial osmolarity of 280-302 mOsm in the light of the Waymoth [IDS-BG] teaching. The cited references are lacking particular disclosure related to the use of CHO cells in the claimed method of culturing animal cells.

The references by Kurano et al. [IDS-BK] and Kurano et al. [IDS-BJ] are relied upon for the disclosure of optimal grow requirements of mammalian cells such as CHO in batch and fed-batch systems.

For example: Kurano et al. [IDS-BJ] teaches a maximum grow rate of CHO cells at lowest glucose concentration of about 0.01-0.25 g/L (see Fig. 3) in batch system and/or a maximum viable cell count at glucose concentration below about 0.5 g/L in fed-batch system (Fig. 6).

And the reference by Kurano et al. [IDS-BK] teaches that the best growth of CHO cells is observed when osmolarity is about 320 mOsm (see abstract).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to substitute CHO cells of the secondary references for mammalian cells in the methods of growing animal cells of the primary references with a reasonable expectation of success in growing CHO cells because optimal and/or best grow conditions for CHO cells with regard to glucose concentration and osmolarity are known in the prior art and these grow conditions are similar to the mammalian cells growth requirements as taught by the cited references. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (703) 308-9351. The examiner can normally be reached on Monday to Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vera Afremova

Art Unit 1651

December 12, 2001.

SANDRA E. SAUCIER
PRIMARY EXAMINER